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REVIEW ARTICLE

Vaccination in special situations

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Abstract

Objectives: To review the indications, contraindications and efficacy of vaccination in some special situations: immunosuppression, prematurity, pregnancy and post-exposure situations.

Sources of data: Systematic review of articles published during the two last decades, found in MEDLINE, SciELO and Lilacs databases; guidelines of *Programa Nacional de Imunizações* (Brazilian National Immunization Program), 2001 to 2004, and of *Programa Nacional de DST/AIDS* (Brazilian National STD/AIDS Program), 2004. Abstracts published in national and international pediatric and infectious disease congress annals during the last five years were also consulted.

Summary of the findings: Some special situations, such as immunosuppression, prematurity, pregnancy and exposure to infectious diseases increased the risk of diseases or adverse post-vaccination events. In these situations, special vaccines or special vaccination schedules are indicated, or vaccines should be postponed or even forbidden. In general, toxoid or inactivated vaccines can be used, considering the possibility of insufficient immune response. For immunosuppressed patients, in accordance with the type of immunosuppression, live virus or bacterial vaccines should be avoided, because of the risk of vaccine agent spread. Immunization should include not only the patient, but his/her home and day-care contacts as well.

Conclusions: Knowledge about the schedule indicated for each situation improves the chances of better vaccine protection and decreases the risk of adverse events. Immunosuppressed or immunodeficient patients whose post-vaccine antibody titers are not available should be considered susceptible when exposed to infectious disease, and all the available prophylactic measures should be implemented, even when the vaccination schedule is correct.

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Generally speaking, vaccination schedules are meant for healthy individuals under normal life conditions. Some special situations, however, place individuals at greater risk of becoming ill or presenting with adverse post-vaccine events and may require specific vaccines or vaccine schemes, or even indicate postponement or contraindication of vaccination.

As follows, we shall discuss some special situations in which the usual vaccine scheme may be modified, postponed or reinforced.

Pre-term newborns

Premature newborns, irrespective of gestational age and birth weight, may receive vaccines in the same scheme and doses used for full term children, except for hepatitis B vaccine.[1] Immunization with hepatitis B vaccine at birth in premature newborns with birth weight under 2,000 g may determine low serum conversion rates; an immunization schedule started at 30 or more days of life determines a response similar to that obtained in full-term newborns with birth weight over 2,000 g.[1,2] Pre-term newborns born to HbsAg-positive mothers or those born to mothers whose HbsAg status is unknown must receive vaccine against hepatitis B and specific hepatitis B immunoglobulin (HBIG) within 12 hours of birth; if the birth weight is under 2,000 g, another three doses of the vaccine must be administered, the first of these at the chronological age of 1 month.

Considering the possibility of prolonged hospitalizations and the risk of invasive bacterial diseases, it is advisable that pre-term newborns should receive pneumococcal conjugate and meningococcal conjugate vaccines, as from 2 months of age; the immunogenicity, efficacy and safety of these vaccines is similar for term and pre-term newborns.[3,4] There are no studies yet about the use of rotavirus vaccine in premature infants.

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Yearly influenza immunization in autumn, as from the age of 6 months, is particularly important for premature infants with chronic pulmonary diseases.[1] Vaccinating family members and other persons that care for the baby is useful, mainly for children under the age of 6 months.

Although there is no absolute contra-indication, the Brazilian National Immunization Program (*Programa Nacional de Imunizações*) postpones the application of BCG vaccine in newborns weighing less than 2,000 g at birth.[5]

Natural breastfeeding and vaccination

No vaccine is contra-indicated or should be postponed in breastfed children – the habitual vaccination scheme must be used. There is also no contra-indication of vaccination for breastfeeding mothers, as the majority of live vaccine agents are not excreted in mother's milk. Although attenuated vaccine virus may be transmitted to the nursing infant through mother's milk in the case of rubella vaccine, this does not determine additional risk for the child.[6]

Vaccination of pregnant women

It is desirable for a woman to be properly immunized before pregnancy starts, but in the event that it is necessary to vaccinate a pregnant woman, the medical, legal and social risks of vaccination at this specific time of life must be assessed, with a view to protecting the pregnant woman and the newborn.[7] Studies have been conducted to seek vaccines which, when applied to pregnant women, are able to induce protection against common and serious diseases in the neonatal period, such as infections by *Streptococcus agalactiae* and *Streptococcus pneumoniae*.[7,8]

When indicated, vaccines containing inactivated viruses or bacteria and toxoid may be applied in pregnant women without risks to the fetus.[9] However, live vaccines are contraindicated during gestation, and women at a fertile age must be guided to avoid pregnancy for 4 week after vaccination with live virus vaccines.[7,9] During a vaccination campaign carried out in the state of São Paulo, Brazil, in the period from November 2001 to February 2002, 811 susceptible pregnant women were inadvertently vaccinated against rubella and it was possible to collect blood samples from 580 newborns of these susceptible women.[10] The congenital infection rate in these newborns was 4.7% (27/580), but no child presented with clinical manifestations of the congenital rubella syndrome. Greater risk of prematurity and low birth weight was however, observed among the infected newborn in comparison with non-infected newborns of susceptible mothers and newborns of immune mothers vaccinated during gestation.[10]

Vaccination with live vaccines to the home contacts of pregnant mothers does not cause any risk to the pregnant women. In situations in which the risk of acquiring disease is greater (for the pregnant mother and/or for the fetus) than the potential risk of the vaccine to the fetus, live oral poliomyelitis vaccines, yellow fever and rabies vaccines may be applied to pregnant women.[1,11,12]

Two vaccines should routinely be offered to pregnant women: tetanus vaccine (with the purpose of preventing neonatal tetanus through passive transplacental antibody passage) and influenza vaccine.[7,11,12] Pregnant women that have completed the tetanus primary immunization schedule must receive a booster dose during pregnancy, in the event that the interval between the last dose of the vaccine and pregnancy is longer than 5 years; non-immunized pregnant women must receive three doses of the vaccine starting as early as possible in the pregnancy; partially vaccinated pregnant women must complete the immunization schedule during gestation.[5] The interval between the first two doses is 2 months, and between the second and third doses, 6 months. If there is no time to apply the three doses of the vaccine during pregnancy, the second dose must be applied at the latest 20 days before the probable date of birth. Every time there is indication of anti-tetanus vaccination, the combined tetanus-diphtheria toxoid vaccine (dT) may be applied to take advantage of the opportunity to protect against diphtheria, since this disease still exists in an endemic form in the country.

Influenza vaccine is recommended for healthy pregnant women with more than 14 weeks of gestation, in the months preceding the influenza season, to diminish the increased risk of severe forms of influenza when pregnant women are hospitalized for this disease; the vaccine is safe throughout pregnancy.[12,13]

Hepatitis A and B vaccines may be applied to susceptible pregnant women who are exposed during gestation.[1,11] Pneumococcal vaccine may be applied to pregnant women with risk of severe disease caused by *S. pneumoniae*.[1] Inactivated polio vaccine (IPV), meningococcal vaccine (conjugate or polysaccharide), oral attenuated or inactivated typhoid fever vaccine can be applied during gestation under special epidemiological conditions (epidemics or journeys to areas where there is increased risk of acquiring the disease).[11,12]

Taking advantage of the puerperal period to vaccinate women susceptible to rubella, measles and other preventable infections by the application of attenuated live virus vaccines is a measure that has great impact on public health.

Vaccinating the immunodeficient child

In the last 3 decades, there has been a considerable

increase in conditions that determine immunodeficiency: organ transplants, immunosuppressive chemotherapy, prolonged use of corticosteroids, HIV infection, among others. An increasing number of children and adults survive these afflictions and become susceptible to infectious agents, thus vaccines are measures capable of actively protecting these patients.

Before indicating immunoprophylaxis for these individuals, the following issues should be carefully assessed: the intensity and duration of immunosuppression, the risks of the disease to be avoided and the benefit (or potential risks) of vaccination, in addition to previous experience with the use of these immunobiologic products in immunosuppressed patients. Generally speaking, vaccines of inactivated and toxoid agents may be applied in a similar manner to that recommended for healthy individuals; live vaccines (viruses or bacteria) should be avoided. Immunization of the household contacts of these patients, especially with live virus vaccines, must also be strictly assessed, considering the possibility of transmission and spread of the vaccine virus, as in the case of OPV.[1] Children undergoing immunoglobulin replacement therapy may not have an adequate response to vaccination; the time interval between immunoglobulin and vaccine application must be assessed for each product used.[12]

Vaccinating the primary immunodeficient child

Immunization is an important active protection instrument against infections in children with congenital immunodeficiencies, but B cell and T cell deficiencies may alter the effectiveness of vaccines and increase the risk of adverse post-vaccine events. Among the congenital immunodeficiencies, severe combined immunodeficiencies are the most feared, as BCG vaccine complications are frequently the first event to indicate this condition.[14] BCG vaccine in these children may determine systemic dissemination of the vaccine bacillus or loco-regional complications.[15] With the purpose of preventing this BCG vaccine complication, which may be fatal, children with a family history suggestive of immunodeficiency (siblings who died prematurely from undefined causes or whose vaccine lesion does not progress normally) must have BCG vaccination postponed until their immunocompetence has been defined.

Oral poliomyelitis vaccine (OPV) (attenuated live virus) must not be applied in children with congenital immunodeficiencies, because of the increased risk of developing paralytic poliomyelitis associated with vaccination, in addition to continuing to excrete the virus for long periods. Severely immunosuppressed patients' home contacts must also not receive this vaccine, because of the risk of vaccine virus dissemination through feces, which may last for up to 4 weeks.[1] Other live virus vaccines, such as measles/rubella/mumps vaccine, and yellow fever vaccine are also contra-indicated for children with T cell immunodeficiency, but there is no contra-indication for applying these vaccines to these patients' household contacts, as the vaccine virus is not disseminated from the vaccinated individual.[1] Attenuated live vaccines against measles, mumps and rubella may be considered for children with slight antibody immunodeficiency.[16]

The varicella vaccine may be applied in children with antibody immunodeficiency, but is contra-indicated in those with cellular immunodeficiency.[17] Vaccinating immunodeficient children's susceptible household contacts, however, is an efficient way to diminish the risk of contact for patients with altered immune response. In the event of post-vaccine cutaneous rash development, the vaccinated individuals must not come into contact with the immunosuppressed patient.

Yearly influenza immunization (before winter) is safe and is indicated in congenitally immunodeficient patients who have greater influenza morbidity and mortality.[13] The vaccine must also be offered to the patient's household contacts, thereby reducing the risk of transmission.

Children with complement deficiency may receive all the vaccines in the routine calendar; there is specific indication for immunization against meningococci, *Haemophilus influenza* type b (Hib) and pneumococci.[18] Children with phagocytosis defects must not receive BCG vaccine, but they may receive the other vaccines in the routine calendar.[19]

The protective response obtained with immunization of those congenital immune deficiency children may be inadequate: the antibody titers obtained may be insufficient, and they may drop more quickly than usual. Thus, even though vaccinated, these patients may remain susceptible to infectious diseases, which make it advisable to perform serologic tests to assess the antibody levels obtained after vaccination; additional or higher doses of vaccines may be necessary and even so, the response obtained may not be optimal. Taking all this into consideration, in the event of exposure to infectious diseases, these patients must be considered susceptible and passive immunization, if available, must be indicated.[16,17]

Vaccinating the child with cancer

The cancer patient must be strictly assessed to verify the immunosuppression conditions dependent on the disease itself, the therapy that the patient is or was submitted to and the risks of the disease one wants to prevent. Live vaccines are formally contra-indicated, and inactivated, sub-unitary, recombining, polysaccharide and toxoid vaccines may be applied, although it is known that the vaccine efficacy may be substantially reduced. The immune response is usually adequate three months to 1

year after chemotherapy has been suspended. When the baseline disease is in remission, and immunosuppressive therapy has been suspended for a period longer than 3 months, the use of live virus vaccines may be considered.[1,16]

Under the following conditions, the vaccine against varicella may be applied in patients with acute lymphoid leukemia:[1,16,17] remission for at least 1 year, peripheral blood lymphocyte and platelet counts higher than 700/mm^3 and 100,000/mm^3, respectively. Two doses should be applied with an interval of 8 weeks between them.

The influenza vaccine[1] must be applied at least 3 to 4 weeks after chemotherapy has been interrupted and when the peripheral granulocyte and lymphocyte counts are higher than 1,000 cells/mm^3. The recommendations for vaccinating the contacts are the same as those made for congenital immunodeficiencies.

Children with cancer are at greater risk of developing invasive Hib disease than immunocompetent children. The more intense and prolonged chemotherapy is, the worse the vaccine response is, thus it is advisable for these patients to receive the vaccine as early as possible after diagnosis and preferably before chemotherapy.[16] For children under the age of 5 years, not previously vaccinated or who received only one dose of the vaccines before they were 12 months old, two doses of the conjugate vaccine are recommended with an interval of 2 months between the doses; those who received two doses of the vaccine before they were 12 months old, must receive only one additional dose of vaccine.[1] Children over the age of 5 years, not previously vaccinated, must receive two doses of the conjugate vaccine, separated by an interval of 1 or 2 months.

In spite of the increased risk of developing *Pneumococcus* invasive disease, the pneumonococcal vaccine may result in sub-optimal protective response in patients with hematologic neoplasias; with the purpose of obtaining protective antibody levels after vaccination, the vaccine must be applied as early as possible after diagnosis, before radiotherapy or chemotherapy begins.[20] Children under the age of 5 years must receive 7-valent conjugate vaccine; children from 2 to 5 years of age that have never been vaccinated should receive two doses of the conjugate vaccine with a 6 to 8 week interval between them, after that, two doses of polysaccharide vaccine: the first dose 6 to 8 weeks after the conjugate vaccine, and the second dose 3 to 5 years after the first polysaccharide vaccine.[20] Children who have had the complete vaccine schedule for their age must receive a booster dose of the conjugate vaccine and two doses of the polysaccharide vaccine with the same interval as before.[20] Children aged between 5 and 10 years receive two doses of polysaccharide vaccine with an interval of 3 years between the doses; over the age of 10 years, they require two doses of the vaccine with an interval of 5 years between doses.[20]

The antibody titers against tetanus, diphtheria and poliomyelitis may be low in cancer patients submitted to chemotherapy; when chemotherapy ends, booster doses of these vaccines must be applied in children and adolescents who have completed the basic vaccination schedule against these diseases.

Vaccination of children with Hodgkin's disease

Patients with Hodgkin's disease may have functional asplenia as a result of the disease or be splenectomized as part of the treatment, and are thus susceptible to disseminated pneumococcal infections. Pneumococcal vaccine must be applied as previously described. The response is better if the vaccine is applied 10 to 14 days before splenectomy or chemotherapy.[16,19] Vaccine applied during or soon after chemotherapy offers the worst results, but the ability to respond with antibody production is rapidly recovered, and may be considered reasonable 3 months after chemotherapy ceases. Patients who receive vaccine during chemotherapy must receive an additional dose 3 months after chemotherapy ends.[1] In these patients, there is also increased risk of developing invasive Hib diseases, and the conjugate vaccine against this agent must be applied.

Children with anatomic or functional asplenia

Anatomic or functional asplenia results in increased risk of developing fulminating bacteremia with high mortality rates.[1] Pneumococci and Hib are the most frequent agents, followed by meningococci, other streptococci and *E. coli*. Pneumococcal conjugate vaccine, meningococcal C conjugate vaccine and Hib vaccine are indicated, in accordance with the same schedule recommended for patients with neoplasias.[21]

Children submitted to bone marrow or solid organ transplants

Vaccination of patients submitted to bone marrow or solid organ transplants must take into consideration the baseline disease, immunosuppressive therapy, donor immunity, time elapsed after transplant and graft versus host reaction.[1] Pneumococcal infections are an important cause of morbidity and mortality after bone marrow transplant, and the risk is greater among patients who present with graft versus host reaction. Protective response is good if the vaccine is applied 6 to 12 months after the transplant and the patient presents with no graft versus host reaction; the response does not change when the donor is vaccinated before the transplant.

Hib is also an important cause of infection in bone marrow transplant patients, but vaccinating the donor before the transplant may induce a good antibody response when the recipient is vaccinated 3 months after the transplant. A single dose of *Hib* conjugate vaccine applied 12 months after the transplant, with a booster dose at 24 months, offers good protection, but it could be used in children in a schedule of four doses at 3, 6, 12 and 24 months after the transplant.[1]

The effectiveness of the vaccine against influenza in this group of patients depends on the space of time that elapses between the transplant and vaccine application: there is no antibody response when this interval is 6 months; 25% of patients respond with antibody production when this interval is from 6 to 12 months, over 60% of patients respond when vaccination is done 2 years after the transplant.[1] Two doses of vaccine with an interval of 1 month between them may be required for a good response. All patients must receive vaccine in the autumn, provided that they received transplants at least 6 months previously.[1] Vaccinating the transplant patient's contacts, including health personnel, is a more efficient measure than vaccinating the patient.

Immunity against tetanus and diphtheria, as is the case with other antibodies, is lost after the transplant. The vaccine schedule with three doses of tetanus-diphtheria vaccine (dT), with an interval of 1 month between doses, starting 12 months after the transplant, is capable of restoring immunity in practically all patients. Vaccinating the donor before the transplant, followed by vaccinating the recipient immediately after the transplant would appear to favor the response of these antigens. However, if a patient suffers tetanogenic injury in the first year after the transplant, s/he must receive hyper-immune anti-tetanus immunoglobulin (TIG), irrespective of having received vaccine in the last three months or not.[1]

Transplanted patients should not receive poliomyelitis live vaccine. When children are exposed to live vaccine virus, by virtue of the routine vaccination of other children, they must receive three doses of the inactivated virus vaccine, although cannot be assured a protective response in all patients.

Not a great deal is known about the immunogenicity of the vaccine against hepatitis B in bone marrow or solid organ transplant patients,[22-24] but, considering the risk of acquiring hepatitis B in blood transfusions, immunization with three doses of the hepatitis B vaccine as from the 12th month after the transplant is indicated. Whenever possible, post-vaccine seroconversion must be assessed, and up to three additional doses of vaccine must be applied in serum negative individuals.[1,22] Serum negative patients who are submitted to solid organ transplants must be vaccinated before the transplant. In the case of chronically dialyzed patients or those with chronic hepatic disease, the vaccine response may not be ideal, and after solid organ transplants, only 5 to 15% of patient seroconvert, which justifies vaccinating them before the transplant.

Whenever possible, vaccines against measles and varicella must be applied at least 1 month before the transplant procedure, since these diseases may determine serious complications in transplant recipients. Measles/mumps/rubella vaccine must be considered 24 months after the transplant, at all times taking into account the epidemiological situation of the disease in the region where the patient is. Patients exposed to disease must receive passive prophylaxis with immunoglobulin.

Varicella vaccine has been used in kidney transplant children with encouraging results,[25] but it has still not been tested in bone marrow transplant recipients. The use of specific varicella-zoster (VZIG) immunoglobulin is indicated for susceptible patients who are exposed to the disease.[1]

BCG vaccine must not be applied to patients submitted to bone marrow or solid organ transplants.

Vaccination of the child receiving corticosteroid therapy

The dose and duration of corticotherapy required to induce immunosuppression in immunocompetent children and adults is still under discussion. In addition to the dose, the frequency, administration route and the underlying disease that originated the corticosteroid therapy indication are important. Doses equal to or higher than 2.0 mg/kg/day of prednisone or 20 mg/day in children weighing over 10 kg (or the equivalent for other corticosteroids), for 14 or more days, have been considered sufficient to counter-indicate live virus vaccines.[1,2] The American Academy of Pediatrics[1] establishes an empirical guide for the application of live virus vaccines in children without underlying immunosuppressive disease on corticotherapy:

- The topical use of corticotherapy, either on the skin or aerosol or intra-articular does not contra-indicate the application of live virus vaccines, except if there is clinical or laboratory evidence of immunodeficiency, in which case immunization must be postponed for up to 1 month after therapy has been discontinued.
- The use of physiological or smaller doses than 2 mg/kg/day of prednisone (or equivalent) does not contra-indicate live virus vaccines.
- Use of doses (daily or on alternate days) equal to or higher than 2 mg/kg/day of prednisone (or equivalent) for periods shorter than 14 days: They may receive live virus vaccines immediately or, if possible, 2 weeks after therapy has been suspended.
- The use of the above-mentioned doses for periods longer than 14 days requires corticotherapy to be

suspended for 1 month before the application of live virus vaccines.

Children with underlying immunosuppressive disease, who receive doses equal to or higher than 2 mg/kg/day of prednisone daily or on alternate days, must not receive live virus vaccines.

HIV-infected children, adolescents and adults

The ideal time to administer vaccines and the possible risks or secondary adverse events of vaccine in patients infected by HIV has not yet been well established. The capacity of HIV-infected individuals to respond with adequate and protective antibody titers after vaccination depends on the degree of immunologic compromise at the time of immunization; for this reason they must be considered as possibly susceptible, even if adequately vaccinated, unless serologic tests have confirmed the presence of adequate antibody titers.[1]

In general, routine vaccination is safe and efficient when applied to children without immunosuppression. Serious complications resulting from immunization with live vaccines in patients infected by HIV have been described with BCG, oral polio and measles vaccines.[1,18,26-29]

It is recommended that vaccines should be applied soon after infection, when the immune response is still adequate and when there is less risk of post-vaccine adverse events. Patients with serious disease and severe immunodepression must have their vaccination postponed whenever possible, until some degree of immune reconstitution is obtained after therapy. Vaccine efficacy, considered insufficient before the use of potent combined antiretroviral therapy (HAART),[30] may be modified by the therapy.

BCG vaccine is recommended at birth in countries with high risk for tuberculosis, such as Brazil, but it is contra-indicated in patients who already present with immunosuppression or clinical signs of the disease.[31] There are still no studies that prove the efficacy and safety of BCG vaccine for protection against tuberculosis in HIV infected children, which makes it difficult to assess the risks and benefits of its application. Although clinical experience has shown good safety of the vaccine in asymptomatic children, regional lymphadenitis may occur, and cases have been described of dissemination of the vaccine bacillus in these children.[32] As the vaccine contains attenuated live mycobacteria, infected children who present with immune reconstitution after HAART has been instituted, may have infection by BCG reactivated long after its application; this reactivation is manifested as abscesses at the vaccine site or in regional lymph nodes.[33] The tuberculin test performed 6 to 12 months after BCG vaccination was not reactive in over 90% of the Brazilian HIV-infected children.[34]

OPV can be applied to HIV-infected children,[35] but preference must be given to IPV, not only for the patients, but for their family members and home contacts as well. In Brazil it is possible to apply IPV in the special immunobiologic reference centers (CRIE). Two cases of post-vaccine paralytic poliomyelitis were described in HIV infected children in Romania and Zimbabwe, but it is not clear whether the occurrence of the paralytic accident in these children was greater than that expected in the general population not infected by HIV.[28,29,36] Symptomatic HIV-infected children or those with severe immunodeficiency must receive only IPV.[31]

Children born to HIV-infected mothers may present reduced placental transfer of antibodies against measles, and be susceptible to natural infection soon after birth.[37] The antibody response after vaccination may be diminished, particularly among symptomatic children with immunosuppression.[37,38] Measles vaccine applied in isolation or in association with rubella and mumps vaccines are safe, and its use has not been associated with greater frequency of adverse events, even in symptomatic individuals.[36] Two cases of measles pneumonitis after vaccination have been described: one adult died[24] and one child recovered.[39] Considering the risk of undesirable adverse events and less protective response, it is recommended that the vaccine be avoided in children with severe immunosuppression.[1,40] HIV-infected adults in our country are usually immune to measles, but in the event that they are susceptible, the vaccine may be applied when there is no severe immunosuppression and there is significant risk of acquiring the disease. If exposed to measles, patients with symptomatic HIV infection, irrespective of their vaccine status, must receive intramuscular standard immunoglobulin in the first 6 days after contact, at the dose of 0.5 mL/kg of weight, up to a maximum dose of 15.0 mL. If children with AIDS, who make regular use of intravenous immunoglobulin, have been in contact with measles, they do not need to make use of prophylactic immunoglobulin, if the last dose of immunoglobulin was administered less than 3 weeks before.[1,41]

No problems have been reported with rubella or its vaccine in HIV-infected children and adolescents. However, Brazilian HIV-infected children present with lower antibody titers and greater chance of remaining susceptible to disease after vaccination at 12 months of age, when compared with seronegative controls, especially when they already present with some degree of immunosuppression at the time of vaccination.[42] Additional doses of vaccine may diminish the contingent of susceptible adolescents, which may indirectly increase the chance of congenital rubella cases.

Varicella may be potentially serious in HIV-infected children and adults. Two doses of the vaccine, with an

interval of 3 months between them, may be applied to asymptomatic or slightly symptomatic children infected by HIV (clinical classification N1 or A1) and who present a T CD4+ lymphocyte percentage higher than or equal to 25%.[17,31,43] Children and adults susceptible to varicella who are exposed to a household, school or in-hospital contact case of varicella must receive VZIG intramuscularly at a dose of 125 U for each 10 kg of weight, with a maximum of 625 U, as quickly as possible after contact, at most within the first 96 hours.[1,41]

The antibody production response against tetanus, diphtheria and Hib would appear to be adequate after primary vaccination in children receiving powerful antiretroviral therapy;[44] there are no contra-indications for vaccination with DTP, dT and the conjugate vaccine against Hib; they are not related to more frequent adverse events and must be applied routinely in HIV+ children. Considering the potential risk of serious bacterial infections in HIV-infected patients, children over the age of 12 months who have not previously been vaccinated against Hib must receive two doses of the vaccine with an interval of 2 months between the doses. The antibody titers against tetanus and diphtheria appear to diminish early in HIV-infected children, particularly those with immunosuppression;[45] additional booster doses may be necessary for these vaccines.[45]

The hepatitis B vaccine is safe for application to HIV-infected children; but only 25 to 50% of vaccinated patients present with protective antibodies;[46,47] this response is better in younger children without immunosuppression. When the hepatitis B vaccine has not been applied in the first year of life and the vaccine schedule is started in symptomatic individuals, a double dose of the vaccine must be applied. A fourth dose of the vaccine must be contemplated.[31,40]

In Brazil, the hepatitis A vaccine is not available to all HIV-infected children; it must be applied to susceptible individuals who present with hepatopathy in a two-dose schedule with an interval of 6 months between them.[40] Research conducted at UNIFESP with children and adolescents exposed to HIV revealed that the prevalence of individuals susceptible to hepatitis A among adolescents is greater than in the non-infected population[48] and that the vaccine is safe and efficient, protecting 100% of the vaccinated HIV-infected children (without severe immunosuppression).[49] Considering that children with AIDS receive antiretroviral therapy that is potentially hepatotoxic, and that hepatitis A virus infection could aggravate HIV infection, vaccine prophylaxis is important for this group of patients.

HIV-infected children and adults must receive annual doses of influenza vaccine, since they are at increased risk of becoming ill and presenting with complications resulting from the influenza. The pneumococcal conjugate vaccine must be applied in the habitual schedule in children that start vaccination in the first months of life (2, 4, 6 and 15 months). Booster doses with polysaccharide vaccine must be applied at 24 and 60 months.[29] Children from 12 to 15 months old with incomplete schemes, or those who have not been vaccinated, receive two doses of conjugate vaccine with an interval of 2 months between the doses and booster doses with polysaccharide vaccine at 24 and 60 months. Children aged between 2 and 10 years receive two doses of polysaccharide vaccine with an interval of 3 months between them. Children over the age of 10 years receive two doses of polysaccharide vaccine with an interval of 5 years between doses.

The efficacy and safety of the yellow fever vaccine in HIV-infected patients has still not been established; it may be applied as from the age of six months of life in endemic areas of the disease, a situation in which the epidemiologic risk justifies indication of the vaccine.[40] According to the Brazilian Ministry of Health guideline, individuals who move to regions of high risk for the disease, and who do not present with immunodeficiency or present it to a moderate degree may receive the vaccine; individuals with a severe degree of immunodeficiency must avoid going to high risk regions and must avoid the vaccine.[31]

Post-exposure vaccination

Infectious disease control includes measures that aim to control the dissemination of disease in the community or in the home. In addition to compulsory notification of some diseases to the epidemiologic surveillance system in order to set control measures in motion, steps must be taken to isolate the patient and prevent or attenuate the disease with the use of antimicrobial agents, immunoglobulin or serums and vaccines.

Here we shall deal with the infectious diseases for which the use of vaccines may prevent infection and the disease, even after exposure.

Mumps

The vaccine against mumps must be administered soon after exposure in unvaccinated exposed children, although there is no evidence that the vaccine prevents the disease from appearing.[50]

Pertussis (whooping cough)

Non-immunized children under the age of 7 years, who have been in contact with pertussis cases, must begin immunization; additional doses of the vaccine to complete the vaccine scheme must be applied in accordance with the regular calendar. Prophylactic antibiotic therapy with azytromicine, erythromycin or clarithromycin must be performed with all contacts, particularly in those under 12 months of age.[51]

Diphtheria

Children exposed to suspected cases of diphtheria, in addition to the other measures (clinical follow-up, antimicrobial agents, oropharynx material culture, etc.) must receive the tetanus-diphtheria vaccine (infant – DT, adult – dT or DTP, depending on age).[52] Children under the age of 7 years must start vaccination, if they have not already been vaccinated, or complete their vaccine calendar, if the scheme is not yet complete. Previously immunized children over the age of 7 years must receive a booster dose of dT, provided that they have not received diphtheria vaccine in the last 5 years.

Hepatitis A

The hepatitis A vaccine has been successfully used in post-exposure prophylaxis to control outbreaks and in home and day care center contacts.[53-55] It must be applied as soon as possible after contact. The use of human immunoglobulin is efficient in post-exposure prophylaxis, when applied up to 2 weeks after contact.[53]

Hepatitis B

Post-exposure prophylaxis must be considered for sexual contacts, home contacts and exposure to blood and derivatives. Perinatal HBV transmission can be prevented in 95% of the newborns to HBsAg+ mothers by active and passive immuno-prophylaxis.[56] Newborns to HBsAg+ mothers must receive hyperimmune human immunoglobulin (HBIG) and vaccine up to 12 hours after delivery; vaccine and HBIG must be administered in different anatomic sites. HBIG must be administered at a dose of 0.5 mL, and the vaccine schedule must be completed with additional doses of the vaccine at 30 days and 6 months; premature newborns weighing under 2,000 g must receive a fourth dose of the vaccine. Newborns to mothers with unknown serology for hepatitis B must also receive vaccine and immunoglobulin soon after birth.[56]

Children under the age of 12 months who do not receive vaccination against hepatitis B and who are in contact at home with HBsAg+ patients must receive HBIG and vaccine; if one or two doses of the vaccine have already been given, the vaccine schedule must be completed.[56] In sexual exposure, the informer must receive HBIG at the dose of 0.06 mL/kg (maximum of 5 mL), up to 14 days from contact and also start a vaccine schedule (0, 1 and 6 months).

Prophylaxis in situations of percutaneous accidents with possibly infected blood depends on the exposed person's vaccine status. Unvaccinated persons must receive HBIG and vaccine; partially vaccinated persons must complete the vaccine scheme.[56]

Meningococci

Careful clinical surveillance and chemo-prophylaxis, preferably in the first 24 hours after exposure to cases of meningococcemia, are mandatory for individuals of any age.[57] The immunization with meningococcal vaccine may be done concurrently with chemo-prophylaxis in outbreak situations, when the serogroup is known and there is an efficient vaccine available, since secondary cases may occur several weeks after the beginning of the index case symptoms.[57]

Measles

The measles vaccine is useful to avoid the appearance of the disease, if administered within 72 hours after contact with a measles case. Therefore, this measure should be implemented as soon as possible.[1] Standard immunoglobulin may be administered as a prophylactic measure up to 96 hours after contact.

Varicella

In susceptible immunocompetent children, the varicella vaccine, when administered up to 72 hours (and possibly up to 120 hours) after contact, may prevent or modify the disease.[2,17] Susceptible children at risk for developing serious forms of varicella, and who cannot receive the vaccine, or who do not receive it in time, must receive VZIG as quickly as possible, up to 92 hours after exposure.[1]

Tetanus

Non-immunized, or incompletely immunized individuals with tetanogenic injuries must receive a dose of the tetanus vaccine, and additional doses must be offered to complete the primary immunization scheme.[5] The need for the simultaneous use of passive immunization depends on the type of injury, the number of doses of the vaccine already received, and the time elapsed since the last dose of the vaccine.[5]

Rabies

In case of exposure to the rabies virus, immediate and careful local treatment must be followed by passive immunoprophylaxis (anti-rabies immunoglobulin) and active immunoprophylaxis (vaccine). The vaccine (obtained in cellular culture) must be applied preferably in the first 24 hours after exposure, but considering the severity of the disease, it must be applied at any time after exposure[58] in five doses on days 0, 3, 7, 14 and 28.[5]

Final considerations

Special situations, in which there is a possibility of insufficient vaccine protective response or greater

occurrence of potentially serious adverse post-vaccine events, must be analyzed individually. Knowledge and use of specific schemes for each situation increase the chance of obtaining a better protective response and diminishing the risk of vaccine related complications.

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